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THE IDENTIFICATION OF ALDEHYDES AND KETONES

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The use of mixed melting points has proved most useful in the qualitative analysis of organic compounds. However, since many organic unknowns are either liquid or amorphous, it is necessary to convert these unknowns into crystalline reference compounds with sharp melting points in a convenient temperature range. The reactions involved in the formation of reference compounds should be rapid and must give reproducible results. Because most aliphatic aldehydes and ketones are liquids unless they are highly substituted, particularly by aromatic radicals, it was recognized early that reference compounds are required in their analysis. This need was especially clear to those engaged in the essential-oil industry.

Although a wide variety of reagents have been utilized to form reference compounds with aldehydes and ketones, only three have found general acceptance—hydroxylamine and two hydrazine derivatives, phenylhydrazine and semicarbazide. Consequently, the older literature and melting-point tables (1) give melting points of oximes, phenylhydrazones, osazones, and semicarbazones. Salts of the reagents were usually used and a standard procedure was developed: Five parts of potassium acetate and three parts of the reagent (as a salt) were mixed in aqueous alcohol. The weakly acidic solution was filtered to remove inorganic salt; one part of the carbonyl compound was added; and the reaction was completed under reflux to form the reference compound.

Although this procedure was satisfactory in a general way, it was far from ideal. The rate of formation is slow; the reaction comes to an equilibrium; and the reference compounds formed separate slowly from solution. Since oximes are often liquids or low-melting solids, hydroxylamine is seldom used, except for quantitative estimation of simple carbonyl compounds.

In attempts to overcome the shortcomings of this procedure, substituted hydrazine derivatives were investigated. Though expensive and of varying stability, some of the substituted derivatives found limited use in certain fields (2). Of these, *p*-nitro and *p*-bromophenylhydrazine and thiosemicarbazide were employed most often. With long aliphatic chains, the spread in melting points between homologous members of a series is reduced, and all the reference compounds of each reagent fall into a range covering about twenty degrees.

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DNPH

Recognizing the need for an inexpensive reagent that would give solid derivatives rapidly with aliphatic compounds, the author called attention to the long-neglected 2,4-dinitrophenylhydrazine (DNPH) (3). It was quickly adopted as a reagent and has since been widely used. This compound has general applicability to the identification of aldehydes and ketones. In acidic solutions, it yields crystalline, colored dinitrophenylhydrazones with good physical properties. Although alcohol is the most common solvent, other solvents, such as acetic acid, pyridine, and "diglyme" (1,2-dimethoxyethane) have been used to increase solubility (4). In a few instances, the proper choice of acid used may favorably affect the results; hydrochloric, sulfuric, perchloric, and phosphoric acids have been used.

The colors of the dinitrophenylhydrazones are of some diagnostic value in identifying the original aldehyde or ketone. Saturated aliphatic compounds give yellow to orange derivatives; unsaturated compounds give red derivatives; aromatic compounds give orange to red derivatives. The infrared and ultraviolet absorption spectra are very useful in identifying the derivatives, particularly in differentiating geometrical isomers (5).

Chromatographic techniques can be applied to the dinitrophenylhydrazones to permit the separation of mixtures and the identification of very small samples (6, 7). DNPH can also be used for the quantitative estimation of many aromatic carbonyl compounds (8) and it is especially useful for acetone and some steroids.

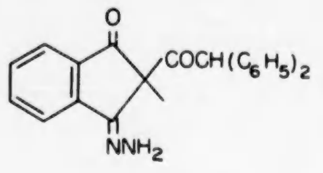
In spite of its wide acceptance, 2,4-dinitrophenylhydrazine has some limitations as a reagent. For example, the hydrazones of DNPH often have polymorphic forms and, in some instances, *cis-trans* isomerism has been observed (5, 9). These properties account for the variations in melting points that have sometimes been reported. In the case of α, β-unsaturated ketones, pyrazolines may be formed, but, since these are also solids, they do not impair the usefulness of the reagent, unless they are difficult to purify.

The fact that dinitrophenylhydrazine reacts with compounds other than aldehydes and ketones is sometimes cited against its use as an analytical tool. But, since reaction conditions for these other compounds are usually sufficiently different from those for aldehydes and ketones, this objection is not serious. Acetals and ketals can be excluded on the basis of prior elemental analyses. DNPH does not react with sugars under the usual conditions, but it does form derivatives after twelve hours of refluxing in absolute alcohol. These derivatives have melting points about twenty degrees above that of the reagent.

Other Hydrazine Reagents

Other poly-substituted hydrazines (e.g., trinitro, trichloro, tribromo) offer little advantage over the 2,4-dinitro reagent, since they yield derivatives whose melting points are only twenty degrees above those obtained with the dinitro reagent; they are more difficult to obtain; and they are more expensive.

However, a new hydrazine-type reagent, 2-diphenylacetyl-1,3-indandione-1-hydrazone (10) (I), has proved useful in the analyses of long-chain carbonyl compounds. As would be expected from its complex structure, this compound gives mixed azines with high melting points. The compounds obtained with I and aliphatic aldehydes have melting points about forty degrees higher than those obtained with DNPH. The melting-point difference is even greater with ketones. How widely it will be adopted remains to be seen.



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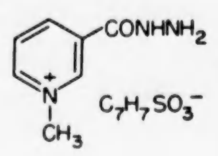

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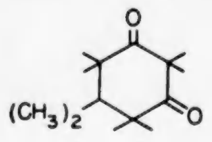

III

Girard's Reagent

In 1936 (11), two new reagents that give water-soluble derivatives were devised in order to isolate carbonyl compounds from mixtures of natural products (steroids). These reagents have become known as Girard's reagent P and Girard's reagent T. They are easily prepared by quaternizing pyridine or trimethylamine with ethyl chloroacetate and treating the product with hydrazine. They are, thus, acethydrazides, solubilized by virtue of the quaternary nitrogen. The reagent and the mixture of unknowns are allowed to interact, after which all unreacted oily material is extracted with ether. Subsequently the carbonyl compound is regenerated. Although the reagent was not designed for identification purposes, the solid derivatives can be isolated and so used. Like dinitrophenylhydrazones, the derivatives can be separated by paper chromatography (6).

To combine the most desirable properties of 2,4-dinitrophenylhydrazine and Girard's reagent, the author (12) devised N-methyl-β-carbohydrazidopyridinium *p*-toluenesulfonate (Methyl Nicotinium *p*-Toluenesulfonate Hydrazide, II). Not only can it be used like Girard's reagent, but the derivatives are easily converted into a 2,4-dinitrophenylhydrazone, so that one aliquot of a carbonyl compound can yield either of two characteristic derivatives. This can be particularly useful for qualitative organic analysis.

Reagents Specific to Aldehydes or Ketones

Reagents which selectively form derivatives with either aldehydes or ketones are useful analytical tools. The aldehyde reagent, Methone (dimedon, dimethyldihydroresorcinol, 5,5-dimethyl-1,3-cyclohexanedione, III), is an outstanding example. Very recently, substituted hydrazines have been described that react selectively with many sugars and show differences among *ortho-*, *meta-*, and *para-*substituted aromatic aldehydes (13). *p*-Hydrazinobenzenesulfonic acid, which reacts only with ketones, has been used to separate ketones from aldehydes. The ketones can then be regenerated by acid hydrolysis (14). *p*-Hydrazinobenzoic acid and carboxymethoxylamine have been used advantageously for the separation of aldehydes from animal tissue (15).

Reagents for Purification

If a reagent is used for the purification of carbonyl compounds, then regeneration from the derivative is essential. This is possible with only a few reagents. Oximes and semicarbazones are most frequently employed for this purpose. As already mentioned, carbonyl compounds can be easily regenerated from the new *p*-toluenesulfonate (12), because the reaction, which is usually carried out in acidic media, is reversible.

2,4-Dinitrophenylhydrazones are unusually difficult to cleave. Two methods have been used for regeneration of the carbonyl compound from which they were

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made. One method consists in treating the derivative under acidic conditions with an excess of a cheap carbonyl compound, or with a carbonyl compound that forms a product that is more insoluble or less readily hydrolyzed. Formaldehyde and pyruvic acid are most often employed (16). In the alternate method, the dinitrophenylhydrazine derivative is destroyed by a reagent that does not attack the released carbonyl compound. Stannous chloride or formic acid and copper carbonate have been employed as reagents. Stannous chloride seems to be the preferable reagent (17).

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